

We claim

1. A substantially purified polypeptide comprising an amino acid sequence according to SEQ ID NO:29.

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2. The substantially purified polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence according to SEQ ID NO: 30.

10 3. The substantially purified polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence according to SEQ ID NO: 31.

4. The substantially purified polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence according to SEQ ID NO: 32.

15 5. The substantially purified polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence according to SEQ ID NO: 33.

6. The substantially purified polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence according to SEQ ID NO: 34.

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7. The substantially purified polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence according to SEQ ID NO: 35.

25 8. The substantially purified polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:98, and SEQ ID NO:100.

30 9. The substantially purified polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence according to the genus R1-R2-R3, wherein

R1 is 0-90 amino acids of SEQ ID NO:35;

R2 is the amino acid sequence according to SEQ ID NO:29; and

R3 is an amino acid sequence selected from the group consisting of SEQ ID NO: 2 and SEQ ID NO:4.

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10. The substantially purified polypeptide of claim 1, wherein the substantially purified polypeptide comprises a polypeptide of the genus X1-X2, wherein:

X1 is 0-90 amino acids of SEQ ID NO:35;

X2 is the amino acid sequence according to SEQ ID NO:29,

10 wherein the polypeptide does not include the sequence of SEQ ID NO:2 or SEQ ID NO:4.

11. A pharmaceutical composition comprising:

(a) a substantially purified polypeptide according to claim 1; and

(b) a pharmaceutically acceptable carrier.

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12. An antibody that selectively binds to the polypeptide of claim 1, but which does not selectively bind to SEQ ID NO:103.

13. A method for making an antibody selective for one or more non-canonical Goodpasture antigen binding protein isoforms, comprising immunizing a host animal with an antigen derived from a polypeptide consisting an amino sequence selected from the group consisting of SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, and isolating antibodies from the host animal that selectively bind to the polypeptide, wherein the isolated antibodies are selective for one or more non-canonical Goodpasture antigen binding protein isoforms, and wherein the isolated antibodies do not selectively bind to SEQ ID NO:103.

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14. An isolated antibody isolated by the method of claim 13.

15. A method for detecting the presence of a protein that is substantially similar to one or more polypeptides comprising an amino acid sequence selected from the group consisting of

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SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, and/or a protein that is substantially similar to one or more polypeptides selected from the group consisting of 60 kDa GPBP, 44-47 kDa GPBP, and 32 kDa GPBP comprise

- a) providing a protein sample to be screened;
- b) contacting the protein sample to be screened with the antibody of claim 14 under conditions that promote antibody-antigen complex formation; and
- c) detecting the formation of antibody-antigen complexes, wherein the presence of the antibody-antigen complex indicates the presence of a protein that is substantially similar to a protein selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, and/or a protein that is substantially similar to one or more polypeptides selected from the group consisting of 60 kDa GPBP, 44-47 kDa GPBP, and 32 kDa GPBP.

16. A substantially purified processed GPBP polypeptide derived from a precursor polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, and/or SEQ ID NO:8 wherein the substantially purified polypeptide is reactive with an antibody selective for one or more epitopes within one or more of the GPBP isoforms disclosed herein, wherein the substantially purified processed GPBP polypeptide is selected from the group consisting of:

- (a) a 60 kDa GPBP with a molecular weight of approximately 60 kDa in denaturing gel electrophoresis, wherein the 60 kDa GPBP is present in lysosomes, cytoplasm, microsomes, and mitochondria in liver tissue, wherein the 60 kDa GPBP is membrane-associated or soluble in the lysosomes in liver tissue;
- (b) a 44-47 kDa GPBP with a molecular weight of approximately 44-47 kDa in denaturing gel electrophoresis, wherein the 44-47 kDa GPBP is present in lysosomes in liver tissue,

wherein the 44-47 kDa GPBP is predominately formed through a leupeptin-sensitive proteolysis in liver tissue; and

(c) a 32 kDa GPBP with a molecular weight of approximately 32 kDa in denaturing gel electrophoresis, wherein the 32 kDa GPBP is present in cytoplasm, mitochondria, microsomes, and lysosomes in liver tissue, and wherein the 32 kDa GPBP is formed through a leupeptin-insensitive proteolysis in liver lysosomes.

17. A method for making the substantially purified processed GPBP polypeptide of claim 16 comprising:

(a) providing cells that express one or more polypeptide comprising or consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8;

(b) lysing the cells and isolating one or more fractions of the cells comprising fractions selected from the group consisting of cytoplasmic-containing fractions, mitochondrial-containing fractions, microsomal-containing fractions, and lysosomal-containing fractions;

(c) contacting the isolated fractions with an immunoaffinity column comprising an antibody that selectively binds to one or more polypeptides comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35 under conditions that result in binding of one or more of the 60 kDa GPBP, the 44-47 kDa GPBP, and the 32 kDa GPBP to the immunoaffinity column;

(d) washing the column under conditions that remove cellular contents that do not selectively bind to the immunoaffinity column;

(e) eluting the bound material from the immunoaffinity column to provide an eluate; and

(f) size fractionating the eluate and isolating one or more of the fractions consisting of the approximately 60 kDa fraction, the approximately 44-47 kDa fraction, and the approximately 32 kDa fraction, wherein the approximately 60 kDa fraction contains the substantially purified 60 kDa

GPBP; the approximately 44-47 kDa fraction contains the substantially purified 44-47 kDa GPBP, and the approximately 32 kDa fraction contains the substantially purified 32 kDa GPBP.

18. A method for making the substantially purified processed GPBP polypeptide of claim 16 comprising:

(a) providing cells that express one or more recombinant polypeptides comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8;

(b) lysing the cells and obtaining a partially purified cell extract containing the recombinant polypeptides;

(c) contacting the partially purified cell extract with liver lysosomal extracts under conditions that promote processing of the recombinant polypeptides to produce a processed extract;

(d) contacting the processed extract with an immunoaffinity column comprising an antibody that selectively binds to one or more epitopes within the recombinant polypeptides and their processed forms comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35 under conditions that result in binding of recombinant polypeptides and their processed forms to the immunoaffinity column;

(e) washing the column under conditions that remove cellular contents that do not selectively bind to the immunoaffinity column;

(f) eluting the bound material from the immunoaffinity column to provide an eluate; and

(g) size fractionating the eluate and isolating one or more of the fractions consisting of the approximately 60 kDa fraction, the approximately 44-47 kDa fraction, and the approximately 32 kDa fraction, wherein the approximately 60 kDa fraction contains the substantially purified 60 kDa GPBP; the approximately 44-47 kDa fraction contains the substantially purified 44-47 kDa GPBP, and the approximately 32 kDa fraction contains the substantially purified 32 kDa GPBP.

19. An isolated polypeptide consisting of the amino acid sequence of SEQ ID NO:38.

20. A method for identifying candidate compounds to treat an autoimmune condition comprising one or more of the following techniques:

(a) incubating a target polypeptide selected from the group consisting of α 3(IV) NC1 domain polypeptide and MBP, and functional equivalents thereof with a GPBP isoform comprising an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28 or a GPBP isoform selected from the group consisting of 60 kDa GPBP, 44-47 kDa GPBP, and 32 kDa GPBP, in the presence of ATP in the presence or absence of one or more test compounds under conditions that promote phosphorylation of the target polypeptide by the GPBP isoform in the absence of the one or more test compounds; detecting phosphorylation of the target polypeptide; and identifying test compounds that reduce phosphorylation of the target polypeptide relative to phosphorylation of the target polypeptide in the absence of the one or more test compounds, wherein such compounds are candidate compounds for treating an autoimmune condition;

(b) incubating a GPBP isoform comprising an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28, or a GPBP isoform selected from the group consisting of 60 kDa GPBP, 44-47 kDa GPBP, and 32 kDa GPBP with ATP in the presence or absence of one or more test compounds under conditions that promote autophosphorylation of the GPBP isoform in the absence of the one or more test compounds; detecting autophosphorylation of the GPBP isoform; and identifying test compounds that reduce autophosphorylation of the GPBP isoform protein relative to autophosphorylation of the GPBP isoform in the absence of the one or more test compounds, wherein such compounds are candidate compounds for treating an autoimmune condition;

(c) incubating a target polypeptide selected from the group consisting of α 3(IV) NC1 domain polypeptide and MBP, and functional equivalents thereof; and a GPBP isoform comprising an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28, or a

GPBP isoform selected from the group consisting of 60 kDa GPBP, 44-47 kDa GPBP, and 32 kDa GPBP; in the presence or absence of one or more test compounds, under conditions that promote conformational isomerization of the target polypeptide catalyzed by the GPBP isoform in the absence of the one or more test compounds, detecting conformational isomerization of the target protein; and identifying test compounds that reduce conformational isomerization of the target protein relative to conformational isomerization of the target protein in the absence of the one or more test compounds, wherein such compounds are candidate compounds to treat an autoimmune condition; and

(d) incubating a GPBP isoform comprising an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28, or a GPBP isoform selected from the group consisting of 60 kDa GPBP, 44-47 kDa GPBP, and 32 kDa GPBP with a target polypeptide selected from the group consisting of α 3(IV) NC1 domain polypeptide and MBP, and functional equivalents thereof, in the presence of one or more test compounds, under conditions that promote formation of an interaction between the GPBP isoform and the target polypeptide in the absence of test compounds and identifying test compounds that inhibit the interaction, wherein such compounds are candidate compounds to treat an autoimmune condition.

21. A method for identifying candidate compounds to treat a protein deposit-mediated disorder comprising one or more of the following techniques:

(a) incubating a target polypeptide selected from the group consisting of α 3(IV) NC1 domain polypeptide, MBP, and prion protein, and functional equivalents thereof with a GPBP protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28 or a GPBP isoform selected from the group consisting of 60 kDa GPBP, 44-47 kDa GPBP, and 32 kDa GPBP, in the presence of ATP in the presence or absence of one or more test compounds under conditions that promote phosphorylation of the target polypeptide by the GPBP in the absence of the one or more test compounds; detecting phosphorylation of the target polypeptide; and identifying test compounds that reduce

phosphorylation of the target polypeptide relative to phosphorylation of the target polypeptide in the absence of the one or more test compounds, wherein such compounds are candidate compounds for treating a protein deposit-mediated disorder;

5 (b) incubating a GPBP isoform comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28 or a GPBP isoform selected from the group consisting of 60 kDa GPBP, 44-47 kDa GPBP, and 32 kDa GPBP, with ATP in the presence or absence of one or more test compounds under conditions that promote
10 autophosphorylation of the GPBP isoform in the absence of the one or more test compounds; detecting autophosphorylation of the GPBP isoform; and identifying test compounds that reduce autophosphorylation of the GPBP isoform relative to autophosphorylation of the GPBP isoform in the absence of the one or more test compounds, wherein such compounds are candidate compounds for treating a protein deposit-mediated disorder;

15 (c) incubating a target polypeptide selected from the group consisting of α 3, MBP, and prion protein, and functional equivalents thereof; and a GPBP isoform comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, and SEQ ID
20 NO:28 or a GPBP isoform selected from the group consisting of 60 kDa GPBP, 44-47 kDa GPBP, and 32 kDa GPBP; in the presence or absence of one or more test compounds, under conditions that promote conformational isomerization of the target polypeptide catalyzed by the GPBP isoform in the absence of the one or more test compounds, detecting conformational isomerization of the target protein; and identifying test compounds that reduce conformational
25 isomerization of the target protein relative to conformational isomerization of the target protein in the absence of the one or more test compounds, wherein such compounds are candidate compounds to treat a protein deposit-mediated disorder; and

(d) incubating a GPBP isoform comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10,
30 SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28 or a GPBP isoform selected from

the group consisting of 60 kDa GPBP, 44-47 kDa GPBP, and 32 kDa GPBP with a target polypeptide selected from the group consisting of α 3, MBP, prion protein, A β 1-42, and functional equivalents thereof, in the presence of one or more test compounds, under conditions that promote formation of an interaction between the GPBP isoform and the target polypeptide in the absence of test compounds and identifying test compounds that inhibit the interaction, wherein such compounds are candidate compounds to treat a protein deposit-mediated disorder.

22. An isolated polypeptide consisting of X1-SHCIX2-X3
wherein X1 is 0-10 amino acids of the sequence ATTAGILATL (SEQ ID NO:41);
X2 is E or Q; and
X3 is 0-10 amino acids of the sequence LMVKREDSWQ (SEQ ID NO:42)

23. An isolated polypeptide consisting of at least 6 amino acids of the sequence EKTAGKPILF (SEQ ID NO:45).

24. A pharmaceutical composition comprising the polypeptide of claim 22 and a pharmaceutically acceptable carrier.

25. A pharmaceutical composition comprising the polypeptide of claim 23 and a pharmaceutically acceptable carrier.

26. An isolated nucleic acid consisting of a sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, and SEQ ID NO:51.

27. A pharmaceutical composition comprising the isolated nucleic acid of claim 26 and a pharmaceutically acceptable carrier.

28. A method for treating a disorder selected from the group consisting of an autoimmune condition and a protein deposit-mediated disorder comprising administering to a subject in need thereof an amount effective of the polypeptide of claim 22 to treat the disorder.

29. A method for treating a disorder selected from the group consisting of an autoimmune condition and a protein deposit-mediated disorder comprising administering to a subject in need thereof an amount effective of the polypeptide of claim 23 to treat the disorder.

30. A method for treating a disorder selected from the group consisting of an autoimmune condition and a protein deposit-mediated disorder comprising administering to a subject in need thereof an amount effective of the nucleic acid of claim 26 to treat the disorder.

31. A method for treating a disorder selected from the group consisting of an autoimmune condition and a protein deposit-mediated disorder comprising administering to a subject in need thereof an amount effective to treat the disorder of a compound selected from the group consisting of staurosporine, Ca^{2+} CaM, 1-[N,O-bis-(5-Isoquinolinesulfonyl)-N-methyl-L-tyrosyl]-4-phenylpiperazine (KN62), and 2-[N-(2-hydroxyethyl)-N-(4-methoxybenzenesulfonyl)]amino-N-(4-chlorocinnamyl)-N-methylbenzylamine (KN-93), or pharmaceutically acceptable salts thereof.

32. A substantially purified polypeptide comprising an amino acid sequence according to GAGAGLLLGCRRVS (SEQ ID NO:101)

33. A substantially purified polypeptide comprising an amino acid sequence at least 80% identical to SEQ ID NO:34.